

Please replace the paragraph beginning on page 4, line 3, with the following rewritten paragraph:

12 --In a preferred embodiment, the subject has an unwanted proliferation of prostate cells, e.g., prostate carcinoma. Preferred treatment includes administering PS and a hormonal agent, e.g., a retinoid or vitamin D, or an agent which increases levels of retinoic acid, e.g., liarozole or Liazal™, to the subject.--

Please replace the paragraph beginning on page 5, line 10, with the following rewritten paragraph:

13 --In another embodiment, the light emitting agent is a PS. In preferred embodiments: the photosensitizer has a chemical structure that includes multiple conjugated rings that allow for light absorption and photoactivation, e.g., the photosensitizer can produce singlet oxygen upon absorption of electromagnetic irradiation at the proper energy level and wavelength. The photosensitizer can include a porphyrin, porphyrin derivative or analog thereof, e.g., a tetraphyrroles; or the photosensitizer can include chlorin e6, a chlorin derivative or analog thereof. Suitable photosensitizers include Photofrin™; synthetic diporphyrins and dichlorins; hydrophorphyrins, e.g., chlorins and bacteriochlorins of the tetra(hydroxyphenyl) porphyrin series; phthalocyanines; O-substituted tetraphenyl porphyrins (picket fence porphyrins); 3,1-meso tetrakis (o-propionamido phenyl) porphyrin; Verdins; Purpurins, e.g., tin and zinc derivatives of octaethylpurpurin (NT2), and etiopurpurin (ET2); Chlorins, e.g., chlorin e6 and mono-1-aspartyl derivative of chlorin e6; Benzoporphyrin derivatives (BPD), e.g., benzoporphyrin monoacid derivatives, tetracyanoethylene adducts of benzoporphyrin, dimethyl acetylenedicarboxylate adducts of benzoporphyrin, Diels-Alder adducts, and monoacid ring "a" derivative of benzoporphyrin; Low density lipoprotein mediated localization parameters similar to those observed with hematoporphyrin derivative (HPD); sulfonated aluminum phthalocyanine (Pc) sulfonated AlPc disulfonated (AlPcS2) tetrasulfonated derivative sulfonated aluminum naphthalocyanines chloroaluminum sulfonated phthalocyanine (CASP); zinc naphthalocyanines; anthracenediones; anthrapyrazoles; aminoanthraquinone; phenoxazine dyes; phenothiazine derivatives; chalcogenapyrylium dyes cationic seleno and tellurapyrylium derivatives; ring-substituted cationic PC; pheophorbide; hematoporphyrin (HP); protoporphyrin; ALA; and ALA esters, hexyl ester or methyl ester.--

Please replace the paragraph beginning on page 7, line 4, with the following rewritten paragraph:

C4  
--The differentiating agent can be, e.g., a hormonal agent, e.g. a retinoid or vitamin D, or an agent which increases levels of retinoic acid, e.g., liarozole or Liaza<sup>TM</sup> retinoic acid; or an antidiabetic compound, e.g., troglitazone, or a ligand for a transcription factor, e.g., transcription factor PPAR gamma.--

Please replace the paragraph beginning on page 11, line 29, with the following rewritten paragraph:

C5  
--Photosensitizers include, but are not limited to, hematoporphyrins, such as hematoporphyrin HCl and hematoporphyrin esters (Dobson, J. and M. Wilson, *Archs. Oral Biol.* 37:883-887); dihematoporphyrin ester (Wilson, M. *et al.*, 1993, *Oral Microbiol. Immunol.* 8:182-187); hematoporphyrin IX (Russell *et al.*, 1991, *Can J. App. Spectros.* 36:103-107, available from Porphyrin Products, Logan, UT) and its derivatives; 3,1-meso tetrakis (*o*-propionamideophenyl) porphyrin; hydroporphyrins such a chlorin, herein, and bacteriochlorin of the tetra (hydroxyphenyl) porphyrin series, and synthetic diporphyrins and dichlorins; *o*-substituted tetraphenyl porphyrins (picket fence porphyrins); chlorin e6 monoethylendiamine monamide (CMA Goff, B.A. *et al.*, 1994, 70:474-480, available from Porphyrin Products, Logan, UT); mono-1-aspartyl derivative of chlorin e6, and mono- and di-aspartyl derivative of chlorin e6; the hematoporphyrin mixture Photofrin<sup>TM</sup> II (Quadra Logic Technologies, Inc., Vancouver, BC, Canada); benzoporphyrin derivatives (BPD), including benzoporphyrin monoacid Ring A (BDP-MA), tetracyanoethylene adducts, dimethyl acetylene dicarboxylate adducts, Diels-Alder adducts, and monoacid ring "a" derivatives; a naphthalocyanine (Biolo, R., 1994, *Photochem. and Photobiol.* 5959:362-365); a Zn(II)-phthalocyanine (Shopora, M. *et al.*, 1995, *Lasers in Medical Science* 10:43-46); toluidine blue O (Wilson, M. *et al.*, 1993, *Lasers in Medical Sci.* 8:69-73); aluminum sulfonated and disulfonated phthalocyanine *ibid.*; and phthalocyanines without metal substituents, and with varying other substituents; a tetrasulfated derivative; sulfonated aluminum naphthalocyanines; methylene blue (*ibid.*); nile blue; crystal violet; azure  $\beta$  chloride and rose bengal (Wilson, M., 1994, *Intl. Dent. J.* 44:187-189). Numerous photosensitizer entitites are disclosed in Wilson, M. *et al.*, 1992, *Curr. Micro.* 25:77-81, and in Okamoto, H. *et al.*, 1992, *Lasers in Surg. Med.* 12:450-485.--

Please replace the paragraph beginning on page 17, line 12, with the following rewritten paragraph:

C16

--The production and purification of light emitting agent:targeting moiety conjugates can be practiced by methods known in the art. Yield from coupling reactions can be assessed by spectroscopy of product eluting from a chromatographic fractionation in the final step of purification. The presence of uncoupled photosensitizer and reaction products containing the photosensitizer can be followed by the physical property that the photosensitizer moiety absorbs light at a characteristic wavelength and extinction coefficient, so incorporation into products can be monitored by absorbance at that wavelength or a similar wavelength. Coupling of one or more photosensitizer molecules to a targeting moiety or to a backbone shifts the peak of absorbance in the elution profile in fractions eluted using sizing gel chromatography, e.g., with the appropriate choice of Sephadex™ G50, G100, or G200 or other such matrices (Pharmacia-Biotech, Piscataway, NJ). Choice of appropriate sizing gel, for example Sephadex™ gel, can be determined by that gel in which the photosensitizer elutes in a fraction beyond the excluded volume of material too large to interact with the bead, i.e., the uncoupled starting photosensitizer composition interacts to some extent with the fractionation bead and is concomitantly retarded to some extent. The correct useful gel can be predicted from the molecular weight of the uncoupled photosensitizer. The successful reaction products of photosensitizer compositions coupled to additional moieties generally have characteristic higher molecular weights, causing them to interact with the chromatographic bead to a lesser extent, and thus appear in fractions eluting earlier than fractions containing the uncoupled photosensitizer substrate. Unreacted photosensitizer substrate generally appears in fractions characteristic of the starting material, and the yield from each reaction can thus be assessed both from the size of the peak of larger molecular weight material, and the decrease in the peak of characteristic starting material. The area under the peak of the product fractions is converted to the size of the yield using the molar extinction coefficient.--

Please replace the paragraph beginning on page 18, line 16, with the following rewritten paragraph:

C17

--Neoplasia involves the loss of normal regulatory mechanisms often associated with the differentiated state. Among a host of strategies to deal with neoplasia, differentiation therapy takes advantage of the fact that normal regulation can sometimes be restored by inducing

C7 terminal differentiation of the cancer cells (*Carducci et al., Seminars in Oncology*. 23:56-62, 1996). The best-known example of differentiation therapy is probably the use of retinoids in acute promyelocytic leukemia. For that particular malignancy, administration of retinoic acid induces immature promyelocytic cells to differentiate along the pathway toward more mature neutrophils, producing cells that are less proliferative and more responsive to adjunctive chemotherapy (*Degos et al., Blood* 85:2643-53, 1995). The newest example of differentiation therapy may be the use of antidiabetic drugs (troglitazone), ligands for the nuclear transcription factor PPAR $\gamma$ , to stimulate terminal differentiation of malignant breast epithelial cells (*Elstner et al., Proc Natl Acad Sci USA* 95:8806-11, 1998 and *Mueller et al. Mol Cell* 1:465-70, 1998). For prostate carcinoma, the notion of differentiation therapy has stemmed from observations that hormonal agents, principally retinoids and vitamin D, can induce differentiation markers in cell lines derived from prostate tumors, e.g., the LNCaP line. Clinically, an agent (liarozole, Liazol<sup>TM</sup>) which promotes cell differentiation by increasing intratumoral levels of retinoic acid is now in early clinical trials, and appears to have some promise for the treatment of prostate cancer. Examples of other differentiation agents include, but are not limited to, polar/apolar compounds such as hexamethylene bisacetamide; vitamin D analogs including 1,25-(OH)<sub>2</sub> D<sub>3</sub>; histone hyperacetylators such as sodium butyrate and prodrugs thereof, sodium propionate and trichostatin A; hormones such as glucocorticoids; antioxidants such as PDTC; peroxisome proliferators such as clofibrate; and miscellaneous differentiating agents such as phenylacetate and phenylbutyrate.--

Please replace the paragraph beginning on page 21, line 25, with the following rewritten paragraph:

C8 --SCID mice bearing (orthotopic) LNCaP tumors were pretreated with a high dose of 400  $\mu$ g/kg R1881 and after 4 days received 250 mg/kg ALA i.p. At 4 hours, the mice were sacrificed and the tumors removed. Frozen section of the tumors were imaged on the confocal laser scanning microscope (CLSM). Using 633 nm excitation, the sections of tumors from an untreated mouse (Figure 5A) and an R1881-pretreated mouse (Figure 5B) were imaged at the same instrument parameters.--

Upon the granting of the attached Petition Under 37 CFR 1.84 Requesting Acceptance of Color Photographs, please insert the following paragraph at page 9, line 12 (after "Brief Description of the Drawing"):